Imaging-based chemical screening reveals activity-dependent neural differentiation of pluripotent stem cells.

Journal: Elife

Publication Year: 2013

Authors: Yaping Sun, Zhiqiang Dong, Taihao Jin, Kean-Hooi Ang, Miller Huang, Kelly M Haston, Jisong Peng, Tao P Zhong, Steven Finkbeiner, William A Weiss, Michelle R Arkin, Lily Y Jan, Su Guo

PubMed link: 24040509

Funding Grants: Common molecular mechanisms in neurodegenerative diseases using patient based iPSC neurons

Public Summary:
The role of mammalian pluripotent stem cells in neurodevelopment and neurodegenerative disorders

Scientific Abstract:
Mammalian pluripotent stem cells (PSCs) represent an important venue for understanding basic principles regulating tissue-specific differentiation and discovering new tools that may facilitate clinical applications. Mechanisms that direct neural differentiation of PSCs involve growth factor signaling and transcription regulation. However, it is unknown whether and how electrical activity influences this process. Here we report a high throughput imaging-based screen, which uncovers that selamectin, an anti-helminthic therapeutic compound with reported activity on invertebrate glutamate-gated chloride channels, promotes neural differentiation of PSCs. We show that selamectin's pro-neurogenic activity is mediated by gamma2-containing GABAA receptors in subsets of neural rosette progenitors, accompanied by increased proneural and lineage-specific transcription factor expression and cell cycle exit. In vivo, selamectin promotes neurogenesis in developing zebrafish. Our results establish a chemical screening platform that reveals activity-dependent neural differentiation from PSCs. Compounds identified in this and future screening might prove therapeutically beneficial for treating neurodevelopmental or neurodegenerative disorders. DOI:http://dx.doi.org/10.7554/eLife.00508.001.